DEPARTMENT OF VETERANS AFFAIRS **8320-01**

38 CFR Part 3

RIN 2900-AR44

Presumptive Service Connection for Rare Respiratory Cancers Due to Exposure to Fine Particulate Matter

AGENCY: Department of Veterans Affairs.

ACTION: Interim final rule.

SUMMARY: The Department of Veterans Affairs (VA) is issuing this interim final rule to amend its adjudication regulations to establish presumptive service connection for nine rare respiratory cancers in association with presumed exposure to fine particulate matter. These presumptions would apply to Veterans with a qualifying period of service, *i.e.,* who served on active military, naval, or air service in the Southwest Asia theater of operations during the Persian Gulf War (hereinafter Gulf War), as well as in Afghanistan, Syria, Djibouti, or Uzbekistan, on or after September 19, 2001, during the Gulf War. This amendment is necessary to implement a decision by the Secretary of Veterans Affairs that determined there is sufficient evidence to support these cancers as presumptive based on exposure to fine particulate matter during service in the Southwest Asia theater of operations, Afghanistan, Syria, Djibouti, or Uzbekistan during certain periods and the subsequent development of the following rare respiratory cancers: squamous cell carcinoma (SCC) of the larynx, SCC of the trachea, adenocarcinoma of the trachea, salivary gland-type tumors of the trachea, adenosquamous carcinoma of the lung, large cell carcinoma of the lung, salivary gland-type tumors of the lung, sarcomatoid carcinoma of the lung, and typical and atypical carcinoid of the lung. The intended effect of this amendment is to ease the evidentiary burden of this population of Veterans who file claims with VA for these nine rare respiratory cancers.

DATES: *Effective date*: This interim final rule is effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

Comment date: Comments must be received on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

Applicability date: The provisions of this interim final rule shall apply to all applications for service connection for squamous cell carcinoma (SCC) of the larynx, SCC of the trachea, adenocarcinoma of the trachea, salivary gland-type tumors of the trachea, adenosquamous carcinoma of the lung, large cell carcinoma of the lung, salivary gland-type tumors of the lung, sarcomatoid carcinoma of the lung, and typical and atypical carcinoid of the lung based on service in the Southwest Asia theater of operations during the Gulf War, as well as Afghanistan, Syria, Djibouti, or Uzbekistan, on or after September 19, 2001, during the Gulf War, that are received by VA on or after the effective date of this interim final rule or that are pending before VA, the United States Court of Appeals for Veterans Claims, or the United States Court of Appeals for the Federal Circuit on the effective date of this interim final rule.

ADDRESSES: Comments may be submitted through www.Regulations.gov. Comments received will be available at regulations.gov for public viewing, inspection, or copies.

FOR FURTHER INFORMATION CONTACT: Jane Allen, Regulations Analyst; Robert Parks, Chief, Regulations Staff (211), Compensation Service (21C), 810 Vermont Avenue, NW., Washington, DC 20420, (202) 461-9700. (This is not a toll-free telephone number.)

SUPPLEMENTARY INFORMATION:

I. Challenges with Rare Cancers

For the purposes of this rulemaking, VA defines rare cancers as cancers with an annual U.S. incidence rate of fewer than 6 cases per 100,000 individuals. This standard

was adopted by an American Cancer Society paper[1] that includes the nine rare respiratory cancers that are being presumptively service connected. The standard has also been adapted internationally; a consortium from the European Union, Surveillance of Rare Cancer in Europe (RARECARE), described the burden of rare cancers in Europe using a revised definition of rare cancers as those with fewer than 6 cases per 100,000 people per year.[2]

Due to low incidence rates, individuals diagnosed with rare cancers face challenges not shared by those diagnosed with more common forms of cancer. Diagnosis often occurs when the cancer has metastasized to other areas of the body. Rare cancers are also more difficult to treat based on limited preclinical research and fewer clinical trials. Prevalence rates are so low that it is unlikely that any epidemiologic or other study will elucidate a cause as may occur with more common cancers. Furthermore, once diagnosed, individuals often struggle to locate information about their cancer, and treatment options are often less effective than for common cancers. As a result of these challenges, five-year relative survival is lower for patients with a rare cancer compared with those diagnosed with a more common cancer among both males (55% vs 75%) and females (60% vs 74%).[3]

II. Presumptive Service Connection Based on Presumed Exposure to Fine Particulate Matter ($PM_{2.5}$)

Particulate matter (PM) (also called particle pollution) is a form of air pollution consisting of solid particles and liquid droplets. PM is comprised of particles of various sizes, with fine particles ($PM_{2.5}$, particles that have a mean aerodynamic diameter ≤2.5

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[1] DeSantis CE, Kramer JL, Jemal A. The burden of rare cancers in the United States. CA Cancer J Clin. 2017 Jul 8;67(4):261-272.
[2] Gatta G, van der Zwan JM, Casali PG, et al. Rare cancers are not so rare: the rare cancer burden in Europe. Eur J Cancer. 2011;47: 2493-2511.
[3] Carol E. DeSantis MPH, Joan L. Kramer MD, Ahmedin Jemal DVM, PhD (2017) “The Burden of Rare Cancers in America,” CA: A Cancer Journal for Clinicians, 67:4, 261-272, available at *https://doi.org/10.3322/caac.21400*

microns) posing the greatest health concern because they can be inhaled, get deep into the lungs, and potentially enter the bloodstream where they can affect the heart and other organ systems resulting in serious health problems.[4] VA published an interim final rule (86 FR 42724) on August 5, 2021, that established presumptive service connection for asthma, sinusitis, and rhinitis due to presumed exposure to $PM_{2.5}$ during the Gulf War (38 CFR 3.320). VA defines the Gulf War as beginning on August 2, 1990 and there is currently no prescribed end date for the Gulf War (38 CFR 3.2). The interim final rule included a description of several studies by the National Academies of Science, Engineering, and Medicine (NASEM) and National Research Council (NRC) examining the possible contribution of air pollution to adverse health effects among U.S. military personnel serving in the Middle East or their descendants.[5]

Based on studies that described particulates in Southwest Asia[6], VA determined that exposures to such particulate matter could present a health risk to service members. In its prior rulemaking, VA acknowledged the challenges associated with conducting exposure-assessment/health surveillance studies in times of conflict and that that precise or specific information on individual veterans' exposures that would be needed to support more granular policy is generally not available.

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[4] See US EPA, Particulate Matter (PM) Basics, https://www.epa.gov/pm-pollution/particulate-matter-pm-basics.

[5] NASEM, Gulf War and Health Series: Volume 3: Fuels and Products of Combustion (2005), https://doi.org/10.17226/11180 and Volume 11: Generational Health Effects of Serving in the Gulf War (2018), https://doi.org/10.17226/25162. National Research Council, Review of the Department of Defense Enhanced Particulate Matter Surveillance Program Report (2010), https://doi.org/10.17226/12911 *(*examining Department of Defense Enhanced Particulate Matter Surveillance Program (EPMSP) Final Report (2008), https://apps.dtic.mil/sti/pdfs/ADA605600.pdf.) NASEM, Long-Term Health Consequences of Exposure to Burn Pits in Iraq and Afghanistan (2011), https://doi.org/10.17226/13209. NASEM, Respiratory Health Effects of Airborne Hazards Exposures in the Southwest Asia Theater of Military Operations (2020), https://doi.org/10.17226/25837.

[6] *E.g., Summary—Review of the Department of Defense Enhanced Particulate Matter Surveillance Program Report—NCBI Bookshelf (nih.gov); Lindsay T. McDonald et. al, Physical and elemental analysis of Middle East sands from recent combat zones, Am J Ind Med. 2020;63:980-987. Inhalation Toxicology, 2020, VOL. 32, NO. 5, 189-199.* https://doi.org/10.1080/08958378.2020.1766602.*; Johann P. Engelbrecht et al., Characterizing Mineral Dusts and Other Aerosols from the Middle East—Part 1: Ambient Sampling and Part 2: Grab Samples and Re-Suspensions, Inhalation Toxicology, International Forum for Respiratory Research 2009:4:297-326 and 327-336,* https://www.tandfonline.com/doi/full/10.1080/08958370802464273 *and* https://www.tandfonline.com/doi/full/10.1080/08958370802464299.

Prior to establishment of 38 CFR 3.320, VA conducted a supplemental literature review focused on $PM_{2.5}$.[7] The focus on $PM_{2.5}$ was intentional for the following reasons: (1) $PM_{2.5}$ is generated by a variety of sources including smoke from open burn pits, (2) the DoD's Enhanced Particulate Matter Surveillance Program objectively measured in-theater concentrations and documented concentrations of $PM_{2.5}$ that may have exceeded military and national exposure guidelines at deployment locations, and (3) its small diameter facilitates greater deposition deep into the lung with known harmful effects. As discussed further below, VA also conducted a review of claims data in conjunction with the supplemental review.

a. 2010 NRC Report, Review of the Department of Defense (DoD) Enhanced Particulate Matter Surveillance Program

In February 2008 the DoD issued the Department of Defense Enhanced Particulate Matter Surveillance Program (EPMSP) Final Report.[8] The purpose of the study was to provide information on the chemical and physical properties of dust collected at deployment locations. Aerosol and bulk soil samples were collected during a period of approximately one year at 15 military sites—including Djibouti, Afghanistan (Bagram, Khowst), Qatar, United Arab Emirates, Iraq (Balad, Baghdad, Tallil, Tikrit, Taji, Al Asad), and Kuwait (Northern, Central, Coastal, and Southern regions). The EPMSP report found that exposures in the region may have exceeded military/national exposure guidelines, including EPA's 24-hr NAAQS for $PM_{2.5}$ (see p.4 and p. 8, Figure 4-1).

The NRC independently reviewed DoD's final report in Review of the Department of Defense Enhanced Particulate Matter Surveillance Program Report in 2010.[9] The

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[7] See US EPA, Particulate Matter (PM) Basics, https://www.epa.gov/pm-pollution/particulate-matter-pm-basics.

[8] Department of Defense Enhanced Particulate Matter Surveillance Program (EPMSP) Final Report (2008), https://apps.dtic.mil/sti/pdfs/ADA605600.pdf.

[9] National Research Council, Review of the Department of Defense Enhanced Particulate Matter Surveillance Program Report (2010), https://doi.org/10.17226/12911.

NRC committee highlighted that the EPMSP was one of the first large-scale efforts to characterize particulate matter exposure in deployed military personnel. Despite the practical challenges of conducting this effort in an austere deployment environment, the NRC report found the results of the EMPSP can be viewed as providing sufficient evidence that deployed military personnel endured occupational exposure to a potential hazard to justify implementation of a comprehensive medical-surveillance program to assess particulate matter-related health effects in military personnel deployed to the Southwest Asia theater of operations.

The NRC committee noted the EPMSP's approach and methodological techniques preclude comparison to existing literature on air sampling and limit a full understanding of particulate matter chemical composition. The study also describes the challenges associated with conducting exposure-assessment/health surveillance studies, including related to: the need to have co-deployed medical/public health experts to conduct sampling; limitations in monitoring technologies in harsh environments for which they have not been validated and where they may overestimate concentrations due to bounce-off problems, limitations in DoD's health effects studies, difficulties in characterization of exposure of troops to multiple sources (dust storms, vehicle emissions, and emissions from burn pits), and potential confounding factors (such as smoking). This along with the infrequency of sampling as well as the lack of consideration of other ambient pollutants in the deployment environment make it challenging to fully ascertain the relationship between exposure data and health effects.

Despite these limitations, the NRC committee found that the EPMSP results clearly documented that service members deployed to the Southwest Asia theater of operations "are exposed to high concentrations of particulate matter and that the particle composition varies considerably over time and space." Further, the NRC Report committee concluded that "it is indeed plausible that exposure to ambient pollution in

the Middle East theater is associated with adverse health outcomes." The health outcomes noted may occur both during service (acute) as well as manifest years after exposure (chronic).

b. 2011 NASEM Report, Long-Term Consequences of Exposure to Burn Pits in Iraq and Afghanistan

To further address and investigate service member exposures, VA requested that NASEM examine the long-term health consequences of service members' exposure to open burn pits while serving in Iraq and Afghanistan. In NASEM's report, Long-Term Consequences of Exposure to Burn Pits in Iraq and Afghanistan, published in 2011, NASEM concluded that particulate matter from regional sources was of potential importance.[10] The report also recommended that VA expand its research studies beyond burn pits to explore the role of a broader range of possible airborne hazards.

c. 2020 NASEM Report: Respiratory Health Effects of Airborne Hazards Exposures in the Southwest Asia Theater of Military Operations

In September 2018, the VA Post Deployment Health Services (PDHS), now called Health Outcomes Military Exposures (HOME), asked NASEM to study the respiratory health effects of airborne hazards exposures in Southwest Asia. On September 11, 2020, NASEM published its findings and recommendations in the report, Respiratory Health Effects of Airborne Hazards Exposures in the Southwest Asia Theater of Military Operations.[11] According to the report, "[b]ased on the epidemiologic studies of military personnel and veterans reviewed in this and previous National Academies reports, the committee concludes that there is inadequate or insufficient

[10] NASEM, Long-Term Health Consequences of Exposure to Burn Pits in Iraq and Afghanistan (2011), https://doi.org/10.17226/13209
[11] NASEM, Respiratory Health Effects of Airborne Hazards Exposures in the Southwest Asia Theater of Military Operations (2020), *https://doi.org/10.17226/25837.*

evidence of an association between airborne hazards exposures in the Southwest Asia theater and the subsequent development of respiratory cancers. While data exist on 1990–1991 Gulf War veterans, the committee notes that no studies have been published concerning those who participated in the post-9/11 conflicts and that—even if such studies were available—the amount of time since exposure may only now be long enough to justify new incidence studies of respiratory cancers in this cohort."

More generally, the 2020 NASEM report identified that existing studies were limited in the available data for exposure estimation; the availability of pertinent health, physiologic, behavioral, and biomarker data, especially data collected both pre- and post-deployment; the amount of time that passed since exposure; and use of additional or alternate sources of data that might enrich analyses. The NASEM committee, noting that the limitations in data quality prevented scientific determinations regarding health outcomes, recommended that a new approach was needed to allow researchers to better examine and respond to whether specific respiratory outcomes are associated with deployment.

III. VA's Identification of Nine Rare Respiratory Cancers Through a Review of Data from NIH/Office of Rare Disease Research

Following publication of the interim final rule (86 FR 42724) mentioned above, VA began a focused review of the scientific and medical evidence related to exposure to $PM_{2.5}$ and the subsequent development of rare respiratory cancers. VA initiated this review to address the needs of veterans diagnosed with rare cancers.

VA's HOME office obtained publicly available data on rare cancers from the Office of Rare Disease Research, National Center for Advancing Translational Sciences (NCATS), in the National Institute of Health (NIH). The data was then cross-referenced with data from the 2017 publication, *The Burden of Rare Cancers in America*. This 2017 study analyzed rare cancers in the United States using invasive cancers found on the

RARECARE list. The RARECARE list is a rare cancer surveillance list based in Europe that is often used by US researchers.[12] The HOME office found 181 rare cancers with less than 6/100,000 incidence and 13 very rare cancers with less than 25 cases in 5 years. The incidence data came from the North American Association of Central Cancer Registries and the Surveillance, Epidemiology, and End Results (SEER) program, both resources from the National Cancer Institute within NIH. A secondary source were data from the Office of Rare Disease Research, NCATS; NIH. These data listed 275 rare diseases and includes mainly cancers with available genetic data. This information matches closely with a public list of rare diseases on the NIH's The Genetic and Rare Diseases Information Center (GARD) website.[13] Rare cancers present in pediatric populations, or that are developmental, genetic, syndromic, or congenital were excluded. This reduced the list to 153 rare cancers after duplicates were removed.

VA noted then that there were nine rare cancers of the respiratory tract: squamous cell carcinoma (SCC) of the larynx, SCC of the trachea, adenocarcinoma of the trachea, salivary gland-type tumors of the trachea, adenosquamous carcinoma of the lung, large cell carcinoma of the lung, salivary gland-type tumors of the lung, sarcomatoid carcinoma of the lung, and typical and atypical carcinoid of the lung. These nine respiratory cancers are exceptionally rare and therefore definitive literature demonstrating an etiology, or lack thereof, is not available and it is not anticipated that it will become available. The HOME office then performed a supplemental literature review of the nine identified rare cancers. Scientific literature on these cancers is extremely limited. The HOME office located and reviewed at least one peer-reviewed source on each rare respiratory cancer (available for download under the "Supporting/Related Materials" section). This literature search demonstrated the paucity

[12] RARECARENet, http://rarecarenet.istitutotumori.mi.it/rarecarenet/
[13] GARD, Genetic and Rare Disease Information Center, https://rarediseases.info.nih.gov/

of other supporting epidemiological or etiologic information from which to derive conclusions on the associations between exposures and the development of these rare respiratory cancers. This does not indicate that there is no connection, it indicates there is not data or published literature to definitively establish a connection.

IV. The Environmental Protection Agency's (EPA) 2019 Integrated Science Assessment (ISA) for Particulate Matter

The EPA is responsible for establishing and periodically reviewing National Air Ambient Quality Standards (NAAQS) for six principal criteria pollutants, which include particulate matter, carbon monoxide, nitrogen dioxide, lead, ozone, and sulfur dioxide to protect public health and welfare. To support this mission, the EPA develops Integrated Science Assessments (ISAs) as part of the periodic review of the NAAQS for each criteria pollutant. The ISAs provide comprehensive reviews of the policy-relevant scientific literature related to the health and welfare effects of a criteria pollutant and form the scientific foundation for each NAAQS review.

The EPA's 2019 ISA for Particulate Matter (2019 PM ISA) provides a thorough evaluation of the scientific evidence pertaining to the relationship between PM exposure, including exposure to $PM_{2.5,}$ and multiple health outcomes, including cancer. Within the discussion of long-term $PM_{2.5}$ exposure and cancer, the 2019 PM ISA evaluates and characterizes the scientific evidence that supports a biologically plausible mechanism by which long-term $PM_{2.5}$ exposure could lead to the development of cancer, such as lung cancer. As noted in Section 10.2 of the 2019 PM ISA: "PM2.5 exhibits several key characteristics of carcinogens (Smith et al., 2016), as shown in toxicological studies demonstrating genotoxic effects, oxidative stress, electrophilicity, and epigenetic alterations, with supportive evidence provided by epidemiologic studies. Furthermore, $PM_{2.5}$ has been shown to act as a tumor promoter in a rodent model of

urethane-initiated carcinogenesis."[14] The body of scientific evidence indicating that $PM_{2.5}$ exhibits multiple characteristics of a carcinogen provides biological plausibility for the generally consistent, positive associations between long-term $PM_{2.5}$ exposure and lung cancer mortality and incidence reported in epidemiologic studies,[15] resulting in the 2019 PM ISA concluding that there is a "likely to be causal" relationship between long-term $PM_{2.5}$ exposure and cancer.

V. Biological Plausibility of Rare Respiratory Cancers

Drawing on conclusions from EPA's 2019 PM ISA for cancer and their evaluation of the evidence for lung cancer incidence and mortality, VA has determined that it is biologically plausible that the mechanisms by which $PM_{2.5}$ may lead to the development of lung cancer can be applied to the development of rare cancers in the lung and can also be applied to development of rare cancers of the respiratory tract. Scientific evidence provides a biologically plausible link by which exposure to $PM_{2.5}$, which often includes some known human carcinogens (e.g., hexavalent chromium, nickel, arsenic, and PAHs), can lead to respiratory tract inflammation as well as genotoxicity (i.e., DNA damage) and epigenetic effects that can result in dysregulated cell growth and ultimately cancer.[16]

VA acknowledges that the epidemiological studies evaluated in the 2019 PM ISA that report generally consistent and positive associations between long-term $PM_{2.5}$ exposures and lung cancer mortality and incidence are not appropriate to extend to the rare cancers under consideration here. As discussed further below, epidemiological data for rare cancers is extremely limited.

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[14] U.S. EPA. Integrated Science Assessment (ISA) for Particulate Matter (Final Report, Dec 2019). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-19/188, 2019, available at http://www.epa.gov/isa.
[15] *Id*. at Figure 10-3 and 10-60.
[16] *Id*.

Additionally, VA's HOME office and Compensation Service analyzed rare respiratory cancer related claims data for Veterans who were deployed to the Southwest Asia theater of operations, as well as Afghanistan, Syria, Djibouti, and Uzbekistan. VA's HOME office and Compensation Service also compared the VBA claims data to data for a similar cohort of Veterans who served during the same period but who had never deployed. Comparison of cohorts showed no meaningful difference between the number of claims received and also no meaningful difference between grant and denial rates. As of September 30, 2021, the VA had received a total of 151 claims for the nine rare respiratory cancers identified by the HOME office from Veterans with Gulf War service.

Although claims data did not demonstrate a significant difference between cohorts, which could be informative with respect to considering a presumption of service connection, VA notes the potential for biological plausibility between airborne hazards, specifically $PM_{2.5}$, and carcinogenesis of the respiratory tract. VA utilized the Bradford Hill criteria to conclude that there were possible relationships with these nine rare cancers and exposure to $PM_{2.5}$. The Bradford Hill criteria are used widely in public health research to establish epidemiologic evidence of a causal relationship between a presumed cause and an observed effect.[17] While there are limited claims data available to suggest otherwise, the nine rare respiratory system cancers were identified as meeting the minimum standard for the Bradford Hill principle of biological plausibility. The remaining Bradford Hill criteria were applied and the nine rare respiratory cancers additionally met the criteria of analogy. VA is employing the analogy of the demonstrable effects of $PM_{2.5}$ on the development of lung cancers to these nine respiratory cancers.

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[17] Kristen M. Fedak, Autumn Bernal, Zachary A. Capshaw, Sherilyn Gross, "Applying the Bradford Hill criteria in the 21st century: how data integration has changed causal inference in molecular epidemiology," *Emerging Themes in Epidemiology*, 12, 14 (2015): doi:10.1186/s12982-015-0037-4

To inform application of these criteria for the nine rare respiratory cancers, VA references analogy between the link between $PM_{2.5}$ and lung cancer. In 2013, the International Agency for Research on Cancer (IARC) classified outdoor air pollution and one of its major components, PM, as carcinogenic. In its evaluation, the IARC identified sufficient evidence showing that exposure to outdoor air pollution and PM causes lung cancer.[18] EPA's 2019 PM ISA also supports the link between particulate matter and lung cancer[19] The VA experts maintain that the Veterans deployed to the Southwest Asia theater of operations, Afghanistan, Syria, Djibouti, and Uzbekistan can reasonably infer exposure to $PM_{2.5}$ can be an etiology for respiratory cancers.

Although VA's HOME office reviewed a number of resources related to rare respiratory cancers (available for download under the "Supporting/Related Materials" section), the literature supporting a link between $PM_{2.5}$ and malignant transformation of cells in other organ systems is as limited as the link to these nine rare respiratory cancers. Thus, based on the scientific evidence providing biological plausibility for lung cancer, VA concluded that it is only biologically plausible that $PM_{2.5}$ exposure could lead to the nine rare respiratory cancers. However, VA is continuing its scientific review of other malignancies, both rare and more common. VA remains committed to cancer surveillance, research and review of peer reviewed science, and plans to review the more robust body of research that exists for more common types of cancers to evaluate the relationship between these cancers and military environmental exposures.

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[18] International Agency for Research on Cancer. *IARC monographs on the evaluation of carcinogenic risks to humans, volume 109. Outdoor Air Pollution.* Lyon, France: IARC; 2013 Available from: https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Outdoor-Air-Pollution-2015.

[19] U.S. EPA. Integrated Science Assessment (ISA) for Particulate Matter (Final Report, Dec 2019). U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-19/188, 2019, available at http://www.epa.gov/isa.

VI. Gulf War Service

In its recent rulemaking, VA established a presumption of exposure to $PM_{2.5}$ for Veterans deployed in the Southwest Asia theater of operations, as defined in 38 CFR 3.317(e)(2), including Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, and the Red Sea during the Gulf War.[20] VA acknowledges that there are important differences between potential exposures experienced by deployed service members and the populations in the studies relied upon by the 2019 PM ISA, and that there are limitations in evidence specific to deployed service members, as discussed above, as well as in the body of evidence surrounding rare respiratory cancers. In the context of regulating potential service connection related to presumed exposure and benefits there is a strong role for policy decisions.[21] The Secretary's broad discretion weighs more strongly here than it would if the science related to the composition and duration of actual particulate matter and airborne hazard exposures of service members were more robust. As discussed further below, an important consideration in establishing these new presumptions for nine rare respiratory cancers is that additional investment in studying these rare cancers is unlikely to fully resolve scientific uncertainty related to service connection due to the small size of the impacted population.

Based on presumed $PM_{2.5}$ exposures and its findings above, VA is establishing a presumption of service connection for the nine rare respiratory cancers, for the service periods and manifestation timelines that follow.

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[20] *See* VA, Presumptive Service Connection for Respiratory Conditions Due to Exposure to Particulate Matter, 86 FR 42724.

[21] *See, e.g.*, VA, Diseases Associated With Exposure to Certain Herbicide Agents (Hairy Cell Leukemia and Other Chronic B-Cell Leukemias, Parkinson's Disease and Ischemic Heart Disease), 75 FR 53202 (where there was only limited/suggestive evidence of an association between Ischemic Heart Disease and service and the Secretary exercised his discretionary authority to grant a presumption of service connection).

VII. Service in Afghanistan, Syria, and Djibouti on or After September 19, 2001

The presumption of exposure to $PM_{2.5}$ also applies to Afghanistan, Syria, and Djibouti for those deployed there on or after September 19, 2001, the earliest date when service members were deployed in these locations.[22] As discussed in the preamble to the interim final rule that established section 3.320, the literature and studies overwhelmingly show the prevalence of $PM_{2.5}$ due to the nature of the arid climate in these locations as well.[23] VA determined that the Southwest Asia theater of operations, Afghanistan, Syria, and Djibouti had similar arid or semi-arid climates with periods of high winds to suspend geologic dusts and regional pollutants, adhered to or a part of these dusts, though the composition of $PM_{2.5}$ varies in different regions. Therefore, VA included Afghanistan, Syria, and Djibouti as qualifying locations for presumption of service connection based on presumed exposure to $PM_{2.5}$.

As the literature and studies overwhelmingly demonstrate the prevalence of $PM_{2.5}$ in these locations, VA included Afghanistan, Syria, and Djibouti in addition to the Southwest Asia theater of operations, as qualifying locations for the presumption of exposure to $PM_{2.5}$ for purposes of service connection for the nine rare respiratory cancers.

VIII. Service in Uzbekistan on or After September 19, 2001

As discussed in the preamble to the interim final rule that established section 3.320, in March 2020, the Army Public Health Center issued, *Environmental Conditions*

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[22] *See id*.

[23] See Lindsay T. McDonald, Steven J. Christopher, Steve L. Morton & Amanda C. LaRue (2020) "Physical and elemental analysis of Middle East sands from recent combat zones," Inhalational Toxicology, 32:5, 189-199, available at https://doi.org/10.1080/08958378.2020.1766602. See UNEP, WMO, UNCCD (2016) "Global Assessment of Sand and Dust Storms," United Nations Environment Programme, Nairobi, 1-15, 21-24, available at https://uneplive.unep.org/redesign/media/docs/assessments/global_assessment_of_sand_and_dust_storms.pdf.

at Karshi Khanabad (K-2) Air Base, Uzbekistan, to provide information to service members and Veterans on environmental exposures at the K-2 Air Base and the risk of potential long-term adverse health effects related to such deployment.[24] It noted that service members, mostly Army, Air Force, and some Marines, were stationed at the air base Camp Stronghold Freedom from October 2001 to November 2005. This fact sheet referenced the results of three declassified assessments conducted by the DoD, namely the Environmental Site Characterization and an Operational Health Risk Assessment completed in 2001 and follow-up Post-Deployment Occupational and Environmental Health Site Assessments completed in 2002 and 2004. The collective findings of these assessments found the K-2 Air Base often had high levels of dust and other particulate matter in the air, depending upon the season and weather conditions, but also noted significantly high levels of dust during dust storms. The fact sheet concluded that there was inconclusive evidence that there is an increased risk of chronic respiratory conditions associated with military deployment to K-2 Air Base. It was noted that DoD was collaborating with VA and independent researchers to further evaluate the potential long-term health risks related to deployment exposures.

Based on these findings regarding particulate matter exposure at the K-2 Air Base, VA established a presumption of exposure to $PM_{2.5}$ for those service members who were deployed to Uzbekistan on or after September 19, 2001. VA acknowledged that this presumption covers a greater geographic area and time frame than the other studies annotated in this document. However, VA believes this is a Veteran-centric approach that enhances its operational efficiencies by simplifying the decision making necessary for claims adjudication.

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[24] Army Public Health Center, Environmental Conditions at Karshi Khanabad (K-2) Air Base, Uzbekistan, Fact Sheet 64-038-0617, https://phc.amedd.army.mil/PHC%20Resource%20Library/EnvironmentalConditionsatK-2AirBaseUzbekistan_FS_64-038-0617.pdf. (accessed July 30, 2021).

IX. Manifestation Period

When VA established presumptions of service connection for asthma, rhinitis, and sinusitis, to include rhinosinusitis, it imposed a requirement that for such diseases to be presumptively service connected, they must have become manifest to any degree, including non-compensable, within 10 years from the date of separation from military service that includes a qualifying period of service. As explained in the preamble to that rule, that requirement was based on a review of the available scientific and medical evidence, including human and epidemiological studies that showed the manifestation of those conditions did not exceed 10 years.

However, VA is not imposing a manifestation period requirement with respect to the nine rare respiratory cancers. Unlike asthma, rhinitis, and sinusitis, cancers may have varying latency periods and also have longer latency periods, even up to decades. Given the uncertain and potential long latency period between exposure and malignant transformation of these rare cancers, there is no time limit between the Veteran's service and the development of disease for the purpose of this presumption. Thus, VA will presume that the nine rare respiratory cancers are service connected if manifested to any degree (including non-compensable) at any time following separation from a qualifying period of military service.

X. Statutory Provisions

The Persian Gulf War Veterans Act of 1998, Public Law 105-277, (codified at 38 U.S.C. 1118), and the Veterans Programs Enhancement Act of 1998, Public Law 105-368, directed the Secretary of Veterans Affairs to enter into an agreement with NASEM to review and evaluate available scientific evidence regarding associations between illnesses and agents, hazards, or medicine or vaccine to which service members may have been exposed during the Gulf War. NASEM provided biennial

reports to VA assessing whether a statistical association exists between exposure to an agent, hazard, or medicine or vaccine and the onset of diseases. Based on the NASEM reports and all other sound medical and scientific information and analysis available, VA would then determine whether a positive association exists between certain exposures and the occurrence of any disease. 38 U.S.C. 1118 defines “positive association” to mean that the credible evidence for an association is equal to or outweighs the credible evidence against an association. If a positive association existed, VA would publish regulations establishing presumptive service connection for that illness.

The statutory provision at 38 U.S.C. 1118 that outlined the procedure for establishing presumptions based on Gulf War service expired on October 1, 2018. However, 38 U.S.C. 501(a)(1) provides that “[t]he Secretary has authority to prescribe all rules and regulations which are necessary or appropriate to carry out the laws administered by [VA] and are consistent with those laws, including . . . regulations with respect to the nature and extent of proof and evidence and the method of taking and furnishing them in order to establish the right to benefits under such laws.” The Secretary may create presumptions for conditions based on exposure to particulate matter under Congress’ broad delegation of general regulatory authority in 38 U.S.C. 501(a)(1), provided there is a rational basis for the presumptions. *NOVA* v. *Sec'y of Veterans Affairs,* 669 F.3d 1340, 1348 (Fed. Cir. 2012) (“A regulation is not arbitrary or capricious if there is a `rational connection between the facts found and the choice made.' ” (quoting *Motor Vehicle Mfrs. Ass'n. of the U.S.* v. *State Farm Mut. Auto. Ins. Co.,* 463 U.S. 29, 43 (1983)).”

XI. Effective Dates

This rule applies to claims received by VA on or after the effective date of the rule and to claims pending before VA, the United States Court of Appeals for Veterans Claims, and the United States Court of Appeals for the Federal Circuit on that date. This

rule will not apply retroactively to claims previously adjudicated. This will ensure that VA adheres to the provisions of its change of law regulation, 38 CFR 3.114, provides that when pension, compensation, dependency and indemnity compensation is awarded or increased pursuant to a liberalizing law, or a liberalizing VA issue approved by the Secretary or by the Secretary's direction, the effective date of such award or increase will be fixed in accordance with the facts found, and will not be earlier than the effective date of the act or administrative issue. *See also* 38 U.S.C. 5110(g).

Additionally, VA will maintain its consistent historical practice of making new presumptions effective on a prospective basis, both to avoid tension with the legal principles discussed above and for the sake of fairness to other veteran cohorts.

XII. Regulatory Amendment

The Secretary of Veterans Affairs has determined that the available scientific and medical evidence is sufficient to warrant a presumption of service connection for nine rare respiratory cancers due to presumed exposure to $PM_{2.5}$ during the Gulf War. Based on presumed exposure to $PM_{2.5}$, VA is recognizing a presumption of service connection for squamous cell carcinoma (SCC) of the larynx, SCC of the trachea, adenocarcinoma of the trachea, salivary gland-type tumors of the trachea, adenosquamous carcinoma of the lung, large cell carcinoma of the lung, salivary gland-type tumors of the lung, sarcomatoid carcinoma of the lung, and typical and atypical carcinoid of the lung.

The principles guiding the Secretary’s determination include the rarity of the conditions, catastrophic nature of the diseases, biological plausibility, analogy to lung cancer, and the reality that these conditions present a situation where it may not be possible to develop additional evidence one way or another. With respect to the nine rare cancers, the Secretary’s determination is supported by the biological plausibility between airborne hazards, specifically $PM_{2.5}$, and carcinogenesis of the respiratory

tract. This determination also took into consideration the debilitating nature of these rare cancers, and the unique challenges faced by Veterans with a rare respiratory cancer diagnosis.

Additionally, the Secretary found that further research is unlikely to provide more conclusive evidence due to disease rarity. Due to the extremely low incidence rates, rare cancers defy both epidemiologic study and the study of pathophysiologic and potential environmental mechanisms. Published exposure studies are typically case reports. Faced with the challenges posed by conditions that are rare, devastating, and for which there is an argument for biological plausibility, but due to that same rarity may defy the timely development of clearer evidence, the Secretary of Veterans Affairs has opted to resolve the issue in favor of making sure VA does all it can for vulnerable veterans.

Therefore, under the general rulemaking authority at 38 U.S.C. 501(a), the Secretary of Veterans Affairs is establishing presumptive service connection for Veterans who were deployed to the Southwest Asia theater of operations as well as Afghanistan, Syria, Djibouti, or Uzbekistan during certain periods and who subsequently develop any of the following rare respiratory cancers at any time after discharge from military service: squamous cell carcinoma (SCC) of the larynx, SCC of trachea, adenocarcinoma of the trachea, salivary gland-type tumors of the trachea, adenosquamous carcinoma of the lung, large cell carcinoma of the lung, salivary gland-type tumors of the lung, sarcomatoid carcinoma of the lung, and typical and atypical carcinoid of the lung.

To accomplish these changes, VA is renumbering existing paragraphs (a)(3) and (a)(4) as (a)(4) and (a)(5) respectively. VA is inserting a new paragraph (a)(3), which addresses the rare cancers associated with exposure to fine particulate matter as explained in the preamble. New paragraph (a)(3) states that the listed rare cancers will

be service connected if manifested to any degree (including non-compensable) at any time following separation from a qualifying period of military service and lists the nine noted rare cancers. Additionally, because the rare cancers are not subject to a manifestation period, but the chronic diseases listed in paragraph (a)(2) are still subject to the 10-year manifestation period as described in current paragraph (a)(1), VA is moving that 10-year manifestation period requirement from paragraph (a)(1) to paragraph (a)(2). Finally, VA is correcting a clerical error in the introductory text of paragraph (b). The text refers incorrectly refers to diseases listed in paragraph (a)(1), but is being corrected to refer to diseases listed in paragraphs (a)(2) and (3).

VA is committed to improving the delivery of health care and benefits to Veterans affected by exposure to airborne hazards during military service and will continue all cancer surveillance and literature review regarding possible associations of other cancers and respiratory hazards in the Southwest Asia theater of operations, Afghanistan, Syria, Djibouti, and Uzbekistan.

Administrative Procedure Act

Pursuant to 5 U.S.C. 553(b)(B) and (d)(3), VA finds that there is good cause to publish this rule without prior opportunity for public comment and good cause to publish this rule with an immediate effective date. Section 553(b)(B) provides that a regulation may be issued without prior opportunity for public comment when an agency for good cause finds "that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest." It is necessary to immediately implement this interim final rule to carry out the Secretary of Veterans Affairs' decision to address the needs of soon-to-be discharged service members and Veterans who have been exposed to airborne hazards, i.e., $PM_{2.5}$, due to their service in the Southwest Asia theater of operations, Afghanistan, Syria, Djibouti, or Uzbekistan, and who subsequently develop

squamous cell carcinoma (SCC) of the larynx, SCC of the trachea, adenocarcinoma of the trachea, salivary gland-type tumors of the trachea, adenosquamous carcinoma of the lung, large cell carcinoma of the lung, salivary gland-type tumors of the lung, sarcomatoid carcinoma of the lung, or typical and atypical carcinoid of the lung. Delay in the implementation of this rule would be impracticable, unnecessary, and contrary to public interest, particularly to Veterans.

It would be impracticable to provide opportunity for prior notice and comment for this rulemaking because a delay in implementation would require VA to delay disability compensation benefits for Gulf War Veterans claiming these nine respiratory cancers that could be granted under these presumptions. It would be contrary to the public interest because a delay in creation of a presumption of service connection for these nine new diseases (which lowers the evidentiary burden for Veterans who are claiming benefits) would delay access to health care, services, and benefits. Furthermore, Veterans diagnosed with rare respiratory cancers have lower survival rates than those diagnosed with more common cancers and may not be receiving adequate health care due to their lack of service-connected status for their disability. Additionally, with the exception of typical and atypical carcinoid of the lung, which have a better prognosis than other pulmonary malignancy and may have a survival rate of 10 years if diagnosed without delay, all these rare respiratory cancers have a median survival timeframe of well under 5 years. Delays in the diagnosis of these rare cancers may occur due to the fact that these cancers have a wide array of symptoms and due to challenges of diagnostic tests and screening for these cancers, which may affect up to 90% of diagnostic errors for these cancers[25]. Even if diagnosed as early as possible the survival timeframes are grim and the quality of life is universally poor. Due to the catastrophic

[25] Del Ciello, Annemilia et al. “Missed lung cancer: when, where, and why?.” Diagnostic and interventional radiology (Ankara, Turkey) vol. 23,2 (2017): 118-126. doi:10.5152/dir.2016.16187

nature of these rare cancers and the associated short survival periods for people suffering from them, preventing the presumption from going into effect while the public comment process is completed would be extremely detrimental to veterans who are currently afflicted with these rare cancers.

In addition, the new presumptions are entirely pro-claimant in nature. And because VA has a sufficient scientific basis to support the new presumptions, continuing to delay claims that could be granted under the presumption while rulemaking is ongoing would unnecessarily deprive veterans and beneficiaries of benefits to which they would otherwise be entitled and prolong their inability to receive benefits. Additionally, this could create risks to beneficiaries' welfare and health that would be exacerbated by any additional delay in implementation. Due to the complexity and the historical scientific uncertainty surrounding both these issues of airborne hazard exposures and rare respiratory cancers, many veterans who will be affected by this rule have long borne the burden and expense of their disabilities while awaiting the results of research and investigation. Under these circumstances, imposing further delay on their receipt of benefits, potentially at the risk of their welfare and health, is contrary to the public interest.

Finally, the Secretary's decision to pursue presumptions of service connection to ease access to VA benefits for veterans who have been exposed to airborne hazards, i.e., particulate matter, requires immediate effect in light of the COVID-19 pandemic. The economic consequences of the pandemic may have strained the personal resources of many who may benefit from these presumptions. For veterans that are not otherwise eligible for health care, these presumptions could result in needed health care eligibility based on service connection. For this reason, delay in implementation of this rule would be contrary to the public interest.

5 U.S.C. 553(d) also requires a 30-day delayed effective date following publication of a rule, except for "(1) a substantive rule which grants or recognizes an exemption or relieves a restriction; (2) interpretative rules and statements of policy; or (3) as otherwise provided by the agency for good cause found and published with the rule." Pursuant to section 553(d)(3), the Secretary of Veterans Affairs finds for the reasons noted above that there is good cause to make the rule effective upon publication in order to provide benefits and health care to Veterans suffering from these nine rare respiratory cancers without delay.

For the foregoing reasons, and as explained in further detail above, the Secretary of Veterans Affairs is issuing this rule as an interim final rule with an immediate effective date. However, the Secretary of Veterans Affairs will consider and address comments that are received within 60 days of the date this interim final rule is published in the Federal Register.

Executive Orders 12866 and 13563

Executive Orders 12866 and 13563 direct agencies to assess the costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety effects, and other advantages; distributive impacts; and equity). Executive Order 13563 (Improving Regulation and Regulatory Review) emphasizes the importance of quantifying both costs and benefits, reducing costs, harmonizing rules, and promoting flexibility. The Office of Information and Regulatory Affairs has determined that this rule is a significant regulatory action under Executive Order 12866. The Regulatory Impact Analysis associated with this rulemaking can be found as a supporting document at www.regulations.gov.

Regulatory Flexibility Act

The Secretary hereby certifies that this interim final rule will not have a significant economic impact on a substantial number of small entities as they are defined in the Regulatory Flexibility Act (5 U.S.C. 601-612). The certification is based on the fact that no small entities or businesses determine service connection, the rating criteria, or assign evaluations for disability claims. Therefore, pursuant to 5 U.S.C. 605(b), the initial and final regulatory flexibility analysis requirements of sections 603 and 604 do not apply.

Unfunded Mandates

The Unfunded Mandates Reform Act of 1995 requires, at 2 U.S.C. 1532, that agencies prepare an assessment of anticipated costs and benefits before issuing any rule that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million or more (adjusted annually for inflation) in any one year. This interim final rule will have no such effect on State, local, and tribal governments, or on the private sector.

Paperwork Reduction Act (PRA)

This interim final rule contains no provisions constituting a collection of information under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3521).

Assistance Listing

The Assistance Listing numbers and titles for this rule are 64.101, Burial Expenses Allowance for Veterans; 64.102, Compensation for Service-Connected Deaths for Veterans' Dependents; 64.105, Pension to Veterans, Surviving Spouses, and Children; 64.109, Veterans Compensation for Service-Connected Disability; and 64.110, Veterans Dependency and Indemnity Compensation for Service-Connected Death.

Congressional Review Act

Pursuant to Subtitle E of the Small Business Regulatory Enforcement Fairness Act of 1996 (known as the Congressional Review Act) (5 U.S.C. 801 *et seq*.), the Office of Information and Regulatory Affairs designated this rule as not a major rule, as defined by 5 U.S.C. 804(2).

List of Subjects in 38 CFR Part 3

Administrative practice and procedure, Claims, Disability benefits, Health care, Pensions, Veterans.

Signing Authority:

Denis McDonough, Secretary of Veterans Affairs, approved this document on February 28, 2022, and authorized the undersigned to sign and submit the document to the Office of the Federal Register for publication electronically as an official document of the Department of Veterans Affairs.

Jeffrey M. Martin,

Assistant Director,

Office of Regulation Policy & Management,

Office of General Counsel,

Department of Veterans Affairs.

For the reasons stated in the preamble, the Department of Veterans Affairs amends 38 CFR part 3 as set forth below:

PART 3 – ADJUDICATION

Subpart A -- Pension Compensation and Dependency and Indemnity Compensation

1. The authority citation for subpart A continues to read as follows:

Authority: 38 U.S.C. 501(a).

2. Revise § 3.320 to read as follows:

§ 3.320 Claims based on exposure to fine particulate matter.

(a) *Service connection based on presumed exposure to fine particulate matter*--(1) *General.* Except as provided in paragraph (b) of this section, a disease listed in paragraphs (a)(2) and (a)(3) of this section shall be service connected even though there is no evidence of such disease during the period of military service.

(2) *Chronic diseases associated with exposure to fine particulate matter.* The following chronic diseases will be service connected if manifested to any degree (including non-compensable) within 10 years from the date of separation from a qualifying period of military service as defined in paragraph (a)(5) of this section.

(i) Asthma.

(ii) Rhinitis.

(iii) Sinusitis, to include rhinosinusitis.

(3) *Rare cancers associated with exposure to fine particulate matter.* The following rare cancers will be service connected if manifested to any degree (including non-compensable) at any time following separation from a qualifying period of military service as defined in paragraph (a)(5) of this section.

(i) Squamous cell carcinoma of the larynx.

(ii) Squamous cell carcinoma of the trachea.

(iii) Adenocarcinoma of the trachea.

(iv) Salivary gland-type tumors of the trachea.

(v) Adenosquamous carcinoma of the lung.

(vi) Large cell carcinoma of the lung.

(vii) Salivary gland-type tumors of the lung.

(viii) Sarcomatoid carcinoma of the lung.

(ix) Typical and atypical carcinoid of the lung.

(4) *Presumption of exposure*. A Veteran who has a qualifying period of service as defined in paragraph (a)(5) of this section shall be presumed to have been exposed to fine, particulate matter during such service, unless there is affirmative evidence to establish that the veteran was not exposed to fine, particulate matter during that service.

(5) *Qualifying period of service.* The term *qualifying period of service* means any period of active military, naval, or air service in:

(i) The Southwest Asia theater of operations, as defined in § 3.317(e)(2), during the Persian Gulf War as defined in § 3.2(i).

(ii) Afghanistan, Syria, Djibouti, or Uzbekistan on or after September 19, 2001 during the Persian Gulf War as defined in § 3.2(i).

(b) *Exceptions.* A disease listed in paragraph (a)(2) and (3) of this section shall not be presumed service connected if there is affirmative evidence that:

(1) The disease was not incurred during or aggravated by a qualifying period of service; or

(2) The disease was caused by a supervening condition or event that occurred between the Veteran's most recent departure from a qualifying period of service and the onset of the disease; or

(3) The disease is the result of the Veteran's own willful misconduct.

[FR Doc. 2022-08820 Filed: 4/25/2022 8:45 am; Publication Date: 4/26/2022]